

# Investigation of the thoracic aorta in cholesterol embolism by transoesophageal echocardiography

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## Abstract

**Objectives**—To examine the thoracic aorta of patients with severe cholesterol embolism (CE) by transoesophageal echocardiography (TOE).

**Methods**—The thoracic aorta of 20 consecutive patients with CE was compared with that in a control population matched for age and risk factors by TOE. Patients were prescribed steroids after CE was diagnosed. Follow up is reported and compared with results in the literature.

**Results**—Aortic plaques and debris were more common in patients with CE than in the control population ( $p < 0.001$  and  $p < 0.0001$ , respectively). The mean (SD) number of aortic plaques in the CE patients was 2.6 (0.7). This aortic atheroma was found predominantly in the descending aorta. One patient died during a mean (SD) follow up of 24 (10) months.

**Conclusions**—Aortic atheroma, as detected by TOE, should be considered as the main source of CE. In addition, the prognosis in our series, in which steroids were systematically prescribed, is much better than in others reported in the literature.

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Keywords: aortic atheroma; transoesophageal echocardiography; cholesterol embolism

Aortic atheroma has been implicated in stroke and macroscopic peripheral embolism. A link between aortic atheroma and cholesterol embolism (CE), a rarer form of peripheral embolism, has not been reported. CE is caused by the migration of atherosclerotic material. The embolism may appear spontaneously but in most patients it occurs after a well recognised event such as aortic or cardiac catheterisation, cardiac surgery with cardiopulmonary bypass, or thrombolytic treatment.<sup>1-6</sup> The atherosclerotic material is thought to originate from the thoracic or abdominal aorta. To our knowledge, however, only a few case reports have identified the thoracic aorta as the source of CE.<sup>7,8</sup>

The aims of this study were to investigate the thoracic aorta of patients with CE by transoesophageal echocardiography (TOE) and to evaluate the efficacy of steroid treatment in these patients.

## Patients and methods

CE was diagnosed on the basis of combined clinical and biological signs in patients with risk factors for atheroma and the usual triggering

circumstances. A skin or muscle biopsy was performed when possible.

Clinical criteria were defined as: (1) the presence of at least two of three cutaneous signs: livedo reticularis, blue toe syndrome, or distal cutaneous necroses; and (2) severe hypertension or worsening of known hypertension with systolic pressure more than 200 mm Hg and diastolic pressure more than 120 mm Hg. This criterion was not mandatory.

Two of three biological criteria were required: (1) an inflammatory syndrome with an erythrocyte sedimentation rate (ESR) of greater than 60 mm in the first hour with no other known cause; (2) more than 500 eosinophils/ml observed in at least two samples; and (3) renal insufficiency defined as a serum creatinine concentration of either more than 200  $\mu\text{mol/l}$  or an increase of 100  $\mu\text{mol/l}$ .

TOE (HP Sonos 1000; Hewlett Packard) was performed to identify the source of emboli; however, particular attention was focused on the thoracic aorta. All parts of the aorta above the diaphragm were examined. An aortic plaque was thicker than 5 mm. Aortic debris was defined as atherosclerotic mobile elements in the lumen. Such debris was often anchored to an aortic plaque (fig 1). The number of plaques and debris for each patient was noted. All patients had an abdominal ultrasound examination to exclude abdominal aortic aneurysm.

As soon as the diagnosis was completed, all patients with CE were systematically treated with steroids. Oral administration of prednisone was started with an initial dose ranging from 1-1.5 mg/kg/day. This dose was maintained for at least one month. If the ESR dropped, the dose was gradually reduced until discontinuation between the third and sixth months. A randomised study of the treatment was not possible because of the small number of patients.

A control population hospitalised for stroke was investigated during the same period.

## STATISTICS

Continuous variables are expressed as means (SD) unless otherwise indicated and are compared using the Student's  $t$  test;  $p < 0.05$  is considered significant.

## Results

### PATIENTS

Twenty patients (19 men and 1 woman; mean (SD) age 69.3 (5) years) with CE were examined by TOE between January 1994 and November 1996. All patients had cutaneous

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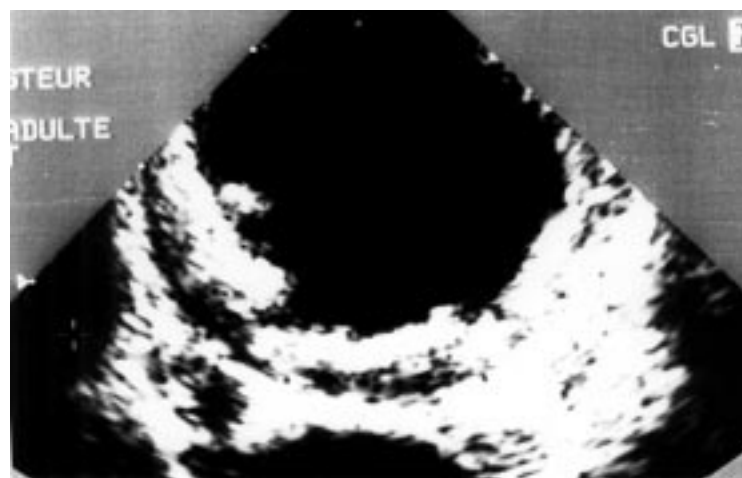


Figure 1 TOE showing aortic plaque with debris on the descending aorta. The atheroma extends into the aortic lumen.

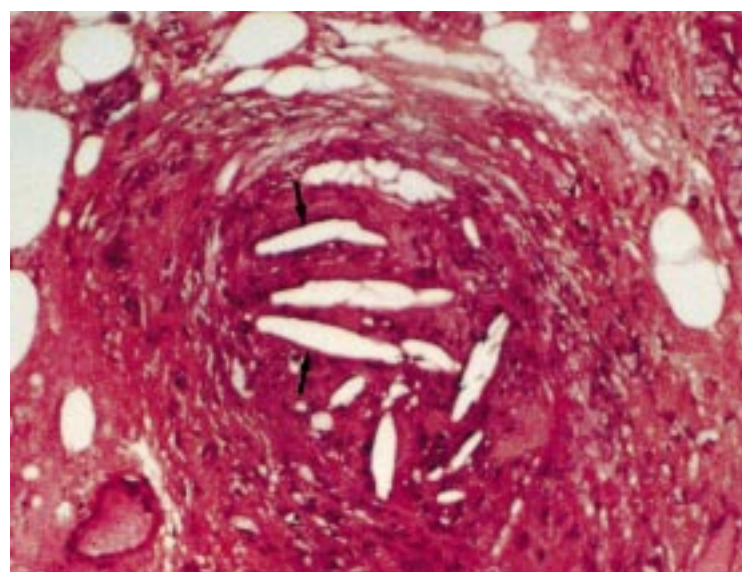


Figure 2 Skin biopsy specimen. Note the small artery in which traces of cholesterol crystals are clearly seen.

signs. Eighteen patients presented with livedo reticularis, blue toe syndrome, and distal ulceration. Two had livedo reticularis and blue toe syndrome. Livedo reticularis involved both lower limbs and the abdomen in 11 patients. Eight patients had severe hypertension requiring antihypertensive treatment. An inflammatory syndrome with an ESR of more than 60 mm in the first hour was seen in all patients. No other known cause that might account for this inflammatory syndrome was found. Hypereosinophilia (greater than 500/ml) was present in at least two samples in 14 patients. Eighteen patients had renal insufficiency as defined previously. The mean (SD) serum creatinine concentration at diagnosis was 285 (124)  $\mu\text{mol/l}$ . A skin or muscle biopsy, or both, was performed on 17 patients and confirmed CE in 14 (fig 2).

In 19 patients CE occurred after cardiac catheterisation or cardiac surgery with aortic clamping, or both. Three of these patients were given thrombolytic treatment for acute myocardial infarction. CE followed carotid angiography in one (table 1). All catheterisa-

Table 1 Patient profiles

Case No	Age (years)	Suspected cause	Time lag* (days)
1	67	CC+CS	(13) 7
2	67	CC	8
3	65	CC+CS	(14) 5
4	72	T+CC	(33) 30
5	78	CC+CS	(15) 6
6	64	CC	5
7	79	CC	12
8	63	T+CC	(12) 8
9	65	CC	7
10	67	CC	8
11	70	CC	28
12	71	CC	6
13	72	CC+S	(15) 7
14	66	CC+CS	(15) 8
15	62	CC	4
16	66	T+CC+CS	(17) (17) 12
17	68	CC	8
18	71	CA	32
19	70	CC	7
20	83	CC	30
Mean (SD)	69.3 (5)		11.1 (9)†

All patients were male except one. In all cases, at least one diagnostic or therapeutic investigation was found to have been performed in the days or weeks preceding the diagnosis.

\*When several potential causes are present, the time lag is the interval between the last causal event and the diagnosis, with the time lag between the preceding potential causal event and CE diagnosis shown in brackets. †Calculated considering the most recent potential cause.

T, thrombolysis; CC, cardiac catheterisation; CS, cardiac surgery; CA, carotid angiography.

tions were performed through a femoral access. No difficulty or particular complication was encountered. The mean (SD) creatinine concentration before catheterisation was 81 (12)  $\mu\text{mol/l}$ . Fourteen patients were treated with anticoagulants (seven with low molecular weight heparin, seven with oral anticoagulants). Seventeen were given antiplatelet treatment (some patients were treated with antiplatelets and anticoagulants).

The mean (SD) latent time between suspected cause (considering the most recent potential cause) and CE diagnosis was 11.1 (9) days. TOE was performed (by one practitioner) with a biplane probe in 18 patients and with a monoplane probe in two.

The control population comprised 36 patients (22 men and 14 women; mean (SD) age 68 (9) years). The main atherosclerotic risk factors in the two groups were similar except for sex (patients with CE being predominantly men).

#### TOE RESULTS

Nineteen (95%) of 20 patients had one or several plaques with a thickness of more than 5 mm. Aortic plaques were located in the descending thoracic aorta in 18 patients. Aortic plaques were seen in the ascending or horizontal thoracic aorta in eight. Seven patients presented with aortic plaques in the descending and ascending aorta. Mobile aortic debris was found in 13 patients, mainly in the descending aorta (12 cases). The mean (SD) number of plaques per patient was 2.6 (0.7) (range 2–4).

Six patients in the control population had an aortic plaque in the descending aorta. One of these patients also had a calcified plaque just above the sigmoid aortic valves. No debris was seen.

Table 2 Comparison of transoesophageal echocardiography investigation between cholesterol embolism patients and control group patients

	Control (n=36)	Cholesterol embolism (n=20)
Aortic plaques (%)	6 (16)	19 (95)*
Aortic debris (%)	0 (0)	13 (65)†

\* $p < 0.001$ , † $p < 0.0001$  cholesterol embolism *v* control group.

The prevalence of aortic plaques and aortic debris is much higher in patients with CE than in those of the control group ( $p < 0.001$  and  $p < 0.0001$ , respectively) (table 2).

#### FOLLOW UP

The inflammatory syndrome regressed with steroid treatment, with a reduction in the sedimentation rate of at least 50% in all patients. The mean (SD) serum creatinine concentration decreased from 285 (124)  $\mu\text{mol/l}$  to 190 (65)  $\mu\text{mol/l}$ .

Steroid treatment was administered for a longer period in two patients who suffered a relapse. The mean (SD) treatment time was 130 (62) days. There were no severe adverse effects, although "cutaneous fragility" was observed in one of the two patients who received a longer period of steroid treatment. No patient was lost over a mean (SD) follow up of 24 (10) months. One patient with severe coronary artery disease died two months after CE was diagnosed.

#### Discussion

CE is a serious and under diagnosed complication of atheroma. When systematic postmortem examination is performed, the prevalence of the disease rises dramatically paralleling the increase in risk factors for atheroma. Consequently, prevalence of 70% has been reported in some series of patients who died following aortic surgery.<sup>9</sup> Several studies have cited aortic atheroma as a potential cause of stroke or macroscopic peripheral emboli.<sup>10-19</sup> None, however, has established a link between aortic atheroma and CE.

In our series the diagnosis of CE is beyond question. Contrast angiography may have been responsible for renal insufficiency. The mean time lag (11 days) between examination and onset of the disease, however, disputes this hypothesis. The time lag was calculated from the day of the last assumed causal event and final diagnosis. When patients were catheterised and then operated on, the time was calculated between the date of surgery and the clinical diagnosis of CE. This long average time lag is partly accounted for by late diagnosis. Most patients had been discharged when the first signs, particularly cutaneous features, were seen. Consequently, CE was diagnosed only several days after the onset of the first clinical signs.

Skin or muscle biopsy specimens were negative in three patients. This findings does not exclude CE, however, as specimens are usually non-contributory in about 30% of patients.<sup>20</sup>

TOE is the most efficient tool for investigating the thoracic aortic wall. The superiority of this imaging method over magnetic resonance

imaging, computed tomography, and angiography is no longer questionable.

Obviously, the abdominal aorta could not be investigated with TOE. The presence of abdominal aortic aneurysm, however, was excluded using ultrasound examination. Downstream migration of abdominal aortic plaques remains possible. The presence of renal insufficiency (90% of patients) as well as the location of the livedo on the upper part of the abdomen (11 patients) suggest that the culprit lesions were upstream of the renal and diaphragmatic arteries.

TOE was used by Karalis *et al*<sup>21</sup> to study patients who underwent invasive aortic procedures. Embolisation occurred during cardiac catheterisation in 15% of 48 patients with protruding atheromas compared with only 3% (two) of 70 patients without protruding atheromas ( $p < 0.05$ ). One patient in two with mobile components to their aortic atheromas suffered from embolic episodes. Several manoeuvres during cardiopulmonary bypass, including over aggressive palpation, aortic cross clamping, anastomosis of the proximal vein grafts, insertion of a cannula, and the "sand-blast" effect of high flow pressure, could explain the dislodgement of material from an atheromatous aorta.<sup>22</sup> But thrombolytic treatment and invasive aortic procedures have also been implicated. As a result, when patients have cardiac catheterisation followed by cardiac surgery or alternatively, thrombolytic treatment followed by cardiac catheterisation or cardiac surgery, or both, it is impossible to determine the exact causal factor. Furthermore, CE may be caused by a combination of several of these trauma. Nevertheless, the diagnosis of CE may be more problematical in postoperative patients who have undergone vein removal for a coronary graft and who often show a slight rise in their serum creatinine concentration.

In our series, prevalence of aortic plaques and debris is much greater than in the control group ( $p < 0.001$  and  $p < 0.0001$ , respectively). The high prevalence of plaques suggests that they are major factors in the aetiology of CE, particularly as they may have been dislodged during iatrogenic intervention.

Does the discovery of these emboligenic sites have any therapeutic implications? The mean (SD) number of plaques per patient was 2.6 (0.7), suggesting the widespread presence of atherosclerosis. It is often difficult to determine which plaque is responsible and, as a result, to envisage clearly targeted intervention—for example, surgery. A course of treatment that stabilises the condition would probably be more appropriate.

The prognosis of patients with CE is generally poor, particularly if renal insufficiency is present. Godeau *et al*<sup>23</sup> reported very high mortality (75%) at six months. This pessimistic prognosis was not found in our patients after a mean follow up of 24 (10) months, although 90% presented with renal insufficiency. Systematic steroid administration possibly explains this positive result. It should be noted, however, that, CE occurred following a well

defined event and may constitute a less severe form than idiopathic CE. Nevertheless, this favourable outcome with steroid treatment will need to be confirmed in a randomised study.

# CONCLUSION

CE, although often misdiagnosed, is probably one of the most common complications of cardiac catheterisation and surgery. Examination of the thoracic aorta in patients with CE, following catheterisation or cardiac surgery, by TOE shows a very high prevalence of severe aortic atheroma with aortic plaques of more than 5 mm in thickness and aortic debris. Ninety five per cent of patients presented with aortic plaque and 65% with aortic debris. This prevalence is much higher than in the control group.

This form of aortic atheroma as detected by TOE should be considered as the source of CE in patients who do not present with aortic aneurysm.

In addition, prognosis of the disease in our series, in which steroid treatment was empirically and systematically prescribed, is much better than in other series reported in the literature. This result should encourage further randomised studies to investigate the effects of steroid treatment.

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